Action of Alkaloidal Extract of *Banisteriopsis quitensis* on Rabbit Ileum

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Abstract □ An alkaloidal extract of *Banisteriopsis quitensis* (Niedenzu) Morton was tested using a rabbit ileum preparation, and inhibition of contractions was noted in untreated strips as well as in those treated with most known stimulants of strip motility. This action was additive with the effect of agents that inhibit strip motility. The activity of the extract was dependent upon intact supplies of calcium in the strip and was diminished by procedures causing depletion of calcium concentration. Loss of calcium from the strip was associated with a pharmacologic response to the extract.

Keyphrases □ *Banisteriopsis quitensis*, alkaloid extract—inhibition of rabbit ileal strip motility, effect of strip calcium content □ Muscular effects—*Banisteriopsis quitensis* extract, rabbit ileal strips

Previous work (1) with an alkaloidal extract of *Banisteriopsis quitensis* (Niedenzu) Morton[1] showed the preparation to have several interesting effects on the CNS, including sedation; passivity of movement; prolongation of hexobarbital "sleeping"times; antagonism of reserpine-induced hypothermia, which was dependent on the presence of serotonin in neural tissue; and analgesia, which was also dependent upon intact neural supplies of serotonin. Ataxia, lordosis, and impaired rotarod performance were seen with the extract, suggesting impairment in motor control or muscular function. Many of the gross effects seen in animals are similar to the effects experienced by South American natives when taking the drug during a tribal ritual (2, 3). Further studies of the effects of the extract on rabbit ileum were completed and are reported here.

EXPERIMENTAL

Effects on Rabbit Ileal Strips—Adult New Zealand White rabbits were sacrificed by a sharp blow to the medullary region of the skull, and a large section of ileum was immediately removed and rapidly divided into 2.5-cm. strips with scissors. As each strip was cut from the ileal section, it was placed into a beaker containing aerated Tyrode's solution, maintained at 37°. Strips were picked at random from the beaker and were placed into muscle bath chambers[2] of approximately 15-ml. capacity, containing Tyrode's solution and having provision for aeration and temperature control of the bath solution. Contractions were recorded[3]; when regular contractions had become established and amplitude had stabilized, drug extract[4] or extract vehicle was introduced into the bath by means of a syringe. Control and experimental strips were run simultaneously, control strips being treated with extract vehicle (7% ethanol) in the same volume as the extract. When pretreatments were used, the full response to the pretreatment was obtained prior to administration of extract or vehicle.

Table I—Calcium Content of Control[a] and Experimental Strips

Control (8 Experiments)	Experimental (7 Experiments)
0.65 ± 0.08[b] mg. Ca/g. wet wt.	0.18 ± 0.013 mg. Ca/g. wet wt.[c]

[a] "Controls" received 1 ml./strip 7% ethanol; "experimentals" received 1 ml./strip alkaloidal extract in 7% ethanol. [b] Standard error of the mean. [c] Difference is significant at $p = 0.025$.

Analysis of Calcium Content of Strips—Rabbit ileal strips were prepared as already outlined. The ileum was divided into alternate "control" and "experimental" strips, and each strip was placed into respective beakers containing aerated, *calcium-free* Tyrode's solution maintained at 37°. Eleven to 15 strips were prepared for each beaker, depending upon the length of ileum obtained. Sample strips were randomly selected from each beaker and placed into the muscle bath chambers, which also contained aerated, calcium-free Tyrode's solution. The volume of solution in the beakers was adjusted so that each beaker contained 15 ml./strip, equivalent to that of the bath chambers. The beakers were kept partially immersed in the circulating bath water and aerated, so that conditions were identical to those in the bath chambers. When maximum amplitudes of contraction had been established, 1 ml. of the drug extract and 1 ml. of the vehicle were added to the respective baths, and 1 ml. of each solution/strip was added to the respective beakers. When a maximum response was noted in the bath containing the extract-treated strip, the strips from each beaker were removed, blotted dry, and weighed, using tared beakers. The strips were digested in boiling H_2SO_4–HNO_3 (1:1 mixture). Digestion was continued until all organic matter had been destroyed, as evidenced by disappearance of charred material and clarification of the solution. The solutions were allowed to cool, divided into three aliquots, and assayed for calcium (4). Results were averaged for each experiment, and Student's t test was applied for statistical analysis.

RESULTS AND DISCUSSION

In preliminary studies, the extract was found to produce inhibition of spontaneous strip activity in volumes as low as 0.1 ml. Complete inhibition of spontaneous activity was usually obtained with 0.5–1.0 ml. of extract/15 ml. of bath volume. Equal volumes of vehicle (7% ethanol) were without effect. The extract produced inhibition of contractions induced by methacholine (0.1–1.0 mg.), serotonin (0.05–1.0 mg.), $BaCl_2$ (0.5–3.0 mg.), pilocarpine (1.0 mg.), nicotine (0.025–1.0 mg.), and $CaCl_2$ (2.0–10.0 mg.). This effect was observed in the presence of phentolamine (0.01–0.2 mg.), propranolol (0.02–0.04 mg.), or both.

The extract produced an inhibition of strip activity which was additive with epinephrine (0.01–0.1 mg.), atropine (0.1–0.5 mg.), $MgCl_2$ (1.25–5.0 mg.), or disodium ethylenediaminetetraacetate (2.0–11.0 mg.). This effect was reversed by the addition of $CaCl_2$

[1] The crude drug was collected from the Ecuadorian basin and was identified by Dr. John D. Dwyer of the Henry Shaw School of Botany, St. Louis, Mo. A voucher specimen is deposited at the Shaw Botanical Garden Herbarium, St. Louis, Mo.

[2] Phipps-Bird, model 7053-400.

[3] Using a Physiograph Six equipped with Isotonic Myographs, Narco Bio-Systems, Houston, Tex.

[4] Representing the alkaloids from 10 mg. crude drug/ml. 7% ethanol. Initial extraction was made using 70% ethanol. Details of the extraction procedure were previously reported (1).

(2.0–10.0 mg.). Prolonged contact with calcium-free Tyrode's solution produced a loss of spontaneous activity and a loss of effect of the extract. This was promptly reversed by the addition of $CaCl_2$ (4.0–10.0 mg.).

It seems likely, from the data, that the extract produces a direct musculotropic effect on strip motility and that this effect is mediated in some way through calcium. Analysis of the calcium content of strips after maximum response to the extract had occurred showed that the calcium content of extract-treated strips was decreased significantly when compared to that of control strips (Table I). This would seem to suggest that at least a part of the action of the extract involves an efflux of calcium from the strip. The question of whether this effect is related to other activities of the extract on the CNS and on skeletal muscle control is a subject for further study.

SUMMARY

This study involved testing an alkaloidal extract of *B. quitensis* on rabbit ileum in the presence of known stimulants and inhibitors of strip motility. Spontaneous contractions were inhibited, as well as those induced by methacholine, serotonin, $BaCl_2$, pilocarpine, nicotine, and $CaCl_2$. The inhibition was additive with inhibition produced by epinephrine, atropine, $MgCl_2$, or disodium ethylenediaminetetraacetate, and it was independent of α- and β-adrenergic receptors. A pharmacologic action involving efflux of calcium from the strips is postulated, based on the dependence upon adequate calcium for effect and the loss of calcium produced during response to the extract.

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Drug Adsorption Efficacy of Commercial Activated Charcoal Tablets *In Vitro* and in Man

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Abstract □ The *in vitro* adsorption characteristics and the inhibitory effect on drug absorption in man of commercial activated charcoal tablets and activated charcoal powder were determined, using phenylpropanolamine as the test drug. The rate and extent of drug adsorption on charcoal in tablets *in vitro* were much lower than on the charcoal powder. Under the conditions of the study, equal doses of charcoal tablets and powder reduced phenylpropanolamine absorption in healthy adult volunteers by 48 and 73%, respectively.

Keyphrases □ Charcoal tablets, activated, commercial—drug adsorption efficacy *in vitro*, in man □ Adsorption characteristics—commercial activated charcoal tablets, *in vitro*, in man □ Activated charcoal tablets—adsorption characteristics, *in vitro*, in man

Activated charcoal, administered as the pure powder dispersed in water, is an effective inhibitor of drug absorption and, therefore, a very useful antidote for many acute poisonings (1–3). The adsorptive capacity of activated charcoal is due mainly to its very large surface area and to the removal of previously adsorbed substances in the activation process. The question arises, therefore, whether or not activated charcoal tablets, which are available commercially, are effective clinically. In theory, the compaction of particles resulting from tablet compression and the addition of other constituents required for producing tablets should diminish appreciably the adsorption efficacy of activated charcoal. Comparative studies have been carried out with commercial tablets and activated charcoal powder, using phenylpropanolamine as the test drug.

EXPERIMENTAL

The activated charcoal tablets used contain 0.33 g. of the adsorbent per tablet and weigh about 0.44 g. each. Comparative studies were carried out with activated charcoal powder USP XVII[1]. Adsorption rates were determined *in vitro* by adding three tablets or 0.5 g. charcoal powder to 50-ml. portions of a 0.25% solution of phenylpropanolamine in 0.1 *N* HCl. These dispersions were agitated by a reciprocating shaker in a water bath at 37°, and three bottles of each were removed periodically for assay. The supernatant solution was filtered rapidly and the filtrate was analyzed for phenylpropanolamine by the method of Heimlich *et al.* (4). Equilibrium adsorption data for Langmuir adsorption isotherms were obtained by methods described previously (2). The disintegration time of the tablets was determined with the USP apparatus without disks in 0.1 *N* HCl at 37°.

Five healthy male volunteers, 22–31 years old, participated in the absorption study. Fifty milligrams of phenylpropanolamine was administered orally in 200 ml. water in the morning on an empty stomach. Charcoal was given immediately thereafter, dispersed in or (in case of the tablets) followed by a similar volume of water. Urine was collected at intervals until no additional drug excretion occurred (about 40 hr.) and was analyzed by the method of Heimlich *et al.* (4).

[1] Norit, American Norit Co., Inc., Jacksonville, Fla.